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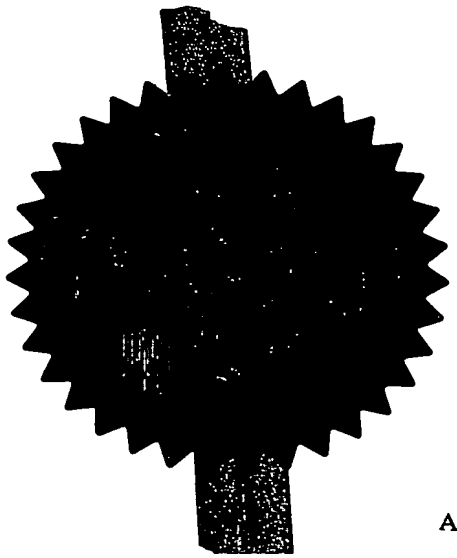

Signed Andrew Gregg

Dated 11 July 2003

Patents Form 1/77

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1/77

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P01/7700 0.00-0308978.6

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

The Patent Office
Cardiff Road
Newport
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1. Your reference — JFR/ND/CB60222P

2. Patent application number
(The Patent Office will fill in his part) — 0308978.6 — 17 APR 2003

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

Glaxo Group Limited
Glaxo Wellcome House, Berkeley Avenue,
Greenford, Middlesex UB6 0NN, Great Britain

Patents ADP number *(if you know it)* 07358700 3

If the applicant is a corporate body, give the country/state of its incorporation — United Kingdom

4. Title of the invention — Formulation

5. Name of your agent *(if you have one)* — Corporate Intellectual Property

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

GlaxoSmithKline
Corporate Intellectual Property (CN9 25.1)
980 Great West Road
BRENTFORD
Middlesex TW8 9GS

Patents ADP number *(if you know it)* 07960982004

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer yes if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is named as an applicant, or
c) any named applicant is a corporate body
See note (d)

Patents Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	8
Claim(s)	
Abstract	
Drawings	

10. If you are also filing any of the following, state how many against each item.

Priority Documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. We request the grant of a patent on the basis of this application

Signature J F Reeves Date 17-Apr-03

12. Name and daytime telephone number of person to contact in the United Kingdom: J F Reeves 020 80474456

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Notes

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Formulation

This invention relates to dentrifice formulations, in particular to a dentrifice formulation that can be stored in a pressurised container from which it can be dispensed onto a toothbrush as a stable controllable foam.

Dentrifices are commonly provided as a paste, i.e. a toothpaste, in a collapsible container from which they can be extruded. It is also known to provide a dentrifice formulation as a foam, e.g. as disclosed in DE-A-100 08 834, DE-A-100 08 836 and DE-A-100 08 837. Such formulations generally comprise a fluid mixture containing one or more abrasive, thickener, flavour etc. together with a propellant, normally a liquefied gas with a boiling point below ambient temperature to drive the formulation out of its container and to expand to form the formulation. The preferred propellant will produce a post-foaming effect.

With this type of formulation it is particularly important to provide a foaming dentifrice that is both practical in use but also gives an immediate visual impact upon dispensing. Japanese Patent Application No.51-12593B discloses a dual phase oil-in-water emulsion formulation for a rapidly collapsing foam aerosol product. The formulation comprises a base agent and a mixed propellant comprising 70-95 wt% dimethylether (DME) and 30-5 wt% water insoluble liquified gas such as a flurocarbon, liquid petroleum, vinyl chloride and methyl chloride. This propellant system is important for products that require a rapid collapsing foam like nail polish or hair spray.

With aerosol dentifrice formulations it is very important to control the production and expansion of foam so that it can be controlled, particularly onto a small surface area toothbrush head. Also, the post-drooling effect on and around the actuator suffered by many aerosol products can lead to unattractive product that becomes unacceptable to use. It is important therefore that the product must not expand further once dispensed onto a toothbrush or suffer from post-drooling effects. With this control and aesthetic appeal the product will be both pleasant and acceptable to the user.

Dentifrice formulations usually contain a high proportion of water and many of the more commonly used propellants, eg, hydrocarbon propellants, are not very miscible with water making the formulation of an acceptable foaming dentifrice

product a challenge for those skilled in the art. As a result, many propellants will not provide acceptable foaming dentifrice formulations, particularly those formulations that are single phase water based. Therefore it is an object of the present invention to provide a foaming dentifrice formulation with a suitable propellant system that produces a very stable foam and avoids all of the above mentioned problems.

According to this invention an aerosol dentrifice formulation is provided comprising a high water based system, a specific particle size abrasive and a liquefied gas propellant, characterised in that the liquified gas comprises 2-8 wt% of a non-hydrocarbon and 2-6 wt% of a hydrocarbon propellant.

Suitable liquified gas propellants include non-hydrocarbon and hydrocarbon propellants. These propellants are well known to those skilled in the art of aerosol formulation.

Suitable non-hydrocarbon propellants include dimethylether (DME), chlorofluorocarbons (CFC's) hydrofluorocarbons (HFC's), hydrochlorofluorocarbons (HCFC's) such as nitrogen, carbon dioxide, nitrous oxide and compressed air. DME is useful as it is a water based propellant.

Suitable hydrocarbon propellants include C_3 to C_5 hydrocarbons (HC's) such as propane, n-butane or butane 22.

Suitable hydrocarbon propellants generate a range of pressures of ca.16-105 psi. Many propellants are known which can achieve this, suitably a commercial product "Butane 30" comprising a mixture of n-butane, i-propane and n-propane. Experiments have shown that when the dentifrice formulation comprises a mixture of hydrocarbon propellant such as n-butane and non-hydrocarbon propellant DME an optimised product is achieved that is particularly stable without any expansion or collapsing of the foam.

Typically a maximum total of 8 wt% propellant is used, more preferably 5 wt%. Preferably the dentifrice formulation of the present invention may comprise between 2-5 wt% of such a liquefied gas propellant mixture.

The formulation is normally stored in a container provided with a release valve, under a pressure corresponding to the vapour pressure of the liquefied

propellant at the storage temperature, and on opening the valve the formulation is expelled as a foam, e.g. onto a toothbrush head.

The abrasive typically comprises 1-10% by weight of the total mixture and has a particle size in the range of between 5-40 microns. Preferably the formulation comprises 9 wt% or less, e.g. 3-7 wt% abrasive, especially 4.5-6 wt%, typically ca. 5 wt%. Preferably the particle size of the abrasive is 30 microns or less, preferably 10 microns or less. Suitably the abrasive material may be a silica. Suitable silicas include those known as Zeodent 124™ and Zeodent 623™. The proportion and particle size of the abrasive are found to optimise the combination of suitability for flow of the formulation out through the valve and effective tooth cleaning.The formulation preferably also contains one or more of the following.

One or more humectant, typically in a proportion of 25-75 wt%, preferably 45-55 wt%, especially 50±2 wt%. Humectants are added to protect the formulation from drying out and to provide consistency and protection against cold. Suitable humectants include sorbitol and glycerol. Suitably a mixture of sorbitol and glycerol may be used e.g. in a sorbitol:glycerol ratio in the range 1:1.5 – 1.5:1. Other humectants may be used including xylitol, mannitol, 1,2-propylene glycol or mixtures of these polyols.

One or more slurrying/suspending agent, typically in a proportion of 1-5 wt%, preferably 2-3 wt%. A preferred slurrying agent is polyethylene glycol, e.g. of molecular weight in the range 200 – 800, typically ca. 300.

One or more foaming agent. Typically a surfactant may be used as a foaming agent. Suitable surfactants include anionic surfactants such as a sodium alkyl sulphate with a 12-18 carbon atoms in the alkyl chain, such as sodium lauryl sulphate. Zwitterionic, ampholytic and non-ionic surfactants may also be used. A mixture of surfactants may be used. Suitably the surfactant may comprise 0.1-3.0 wt% of the formulation, preferably 1-2 wt%.

One or more thickening agent that will add body to the foam. Typical thickening agents include hydroxypropylmethylcellulose (HPMC), hydtrxyethylcellulose (HEC) and hydroxymethylcellulose (HMC) and the acrylic polymer Carbopol. Preferred thickening agents include xanthan gum and/or a thickening silica, Zeodent 163. Typically the thickening agent may comprise 0.1-

4.0 wt% of the formulation, typically 0.2-3.0 wt%. It is found that use of xanthan gum and Zeodent 163 can lead to a creamier foam with improved flow and texture characteristics.

One or more pH regulator, preferably to maintain the pH at 6.0-10.0, especially at ca. pH 8.0. Such a pH is found suitable to avoid corrosion of the tin plate or aluminum containers that may be lacquered that are commonly used for containing such formulations. A suitable pH regulator is sodium hydroxide.

One or more other excipent such as a sweetener, colour, preservative, flavours, dyes etc., typically comprising up to ca. 2 wt% of the formulation.

Such compositions of the present invention may also comprise other active agents conventionally used in dentifrice compositions, for instance:
an antimicrobial agent, anti-plaque agent such as chlorhexidine or triclosan; anti-calculus agent such as a tetra- or a di-alkali metal pyrophosphate salt, or a mixture thereof, an alkali metal tripolyphosphate salt or an azacycloheptane diphosphonate salt; an anti-sensitivity agent such as strontium acetate, strontium chloride or a potassium salt such as potassium nitrate, potassium chloride or potassium citrate; remineralisation agent, a whitening agent such as tetra- or a di-alkali metal pyrophosphate or phosphate salts or peroxides, vitamins, fluoride, e.g. sodium fluoride, typically comprising up to ca. 0.5 wt% of the formulation. Such agents will be included at levels to provide the desired therapeutic effect.

Many other examples of materials of these types are known in the state of the art, e.g. in DE-A-100 08 837, the content of which is incorporated herein by way of example only.

The remainder of the formulation may comprise water, typically comprising ca. 25-50 wt%, preferably 30-40 wt% of the formulation.

A typical formulation according to this invention therefore comprises: one or more humectant 45-55 wt%, slurrying agent 2-3 wt%, foaming agent 1-2 wt%, abrasives 3-7 wt%, preferably 3-5 wt %, thickening agent 0.2-0.5 wt%, flavour, active and sweetener 0-2 wt%, pH adjuster if necessary to provide pH of 8.5+/- 0.2, water 30-40 wt % preferably 35 +/- 1 wt%. This fluid formulation which is also known as the intermediate formulation is preferably charged into a metal

container with a dispensing valve, at a proportion of 95 wt% with 5 wt% propellant mixture providing a pressure of between 25-70, preferably 40-60 psi.

The preferred materials and their proportions described above also contribute to improved flow and handling of the formulation.

The following observations in the finished product were noted:

N butane	0%	2%	2.5%	3%	5%
Dimethylether	5%	3%	2.5%	2%	0%
Observation	Foam which collapses instantly	Stable foam, no expansion or collapse	Very slightly expanding foam	Slightly expanding foam	Very expanding foam

A typical process for making the formulation of this invention may involve the steps of:

1. Adding a suitable quantity of water to a mixing vessel.
2. Adding sweetener and active to the water and agitating until dissolved or suspended.
3. Adding the humectant and agitating until homogeneous.
4. Sieving the abrasive to break up any lumps. A 500 micron sieve is generally suitable.
5. Slowly adding the abrasive to the mixture while mixing.
6. Slurrying the thickening agent and slurrying agent and add to the mixture, agitate until homogeneous.
7. Mixing, optionally transferring to a mixer.
8. Slurrying the flavour, dye and foaming agent and adding to the mixture, mixing until homogeneous.
9. Adjusting the pH.
10. Mixing until homogeneous.

This fluid mixture may then be charged into suitable valued containers together with a suitable quantity of propellant.

The formulation may be used in a generally conventional manner involving opening the valve of the container to allow the internal pressure to expel the formulation onto a toothbrush. The invention also provides a valved container containing a formulation as described above.

The invention will now be described by way of example.

Example 1

A dentrifice formulation was prepared having the following composition:

Function	**Component**	**wt%**
Humectant	Sorbitol 70% non-crystallizing	28.000
Humectant	Glycerin	22.00
Suspending agent	PEG 6	2.500
Foaming agent	Empicol 0303 30% solution	5.000
Sweetener	Sodium saccharin	0.300
Active	Sodium fluoride	0.306
Flavour	Flavour	1.000
Abrasive (hard)	Zeodent 124	1.330
Abrasive (soft)	Zeodent 623	3.670
Thickener	Xanthan (Keltrol F)	0.250
pH adjuster	35% NaOH solution	0.250
Dye	Dye	0.003
Water	to	100.000

Example 2

Function	**Component**	**wt%**
Humectant	Sorbitol 70% non-crystallizing	28.000
Humectant	Glycerin	22.00
Suspending agent	PEG 6	2.500
Foaming agent	Empicol 0303 30% solution	5.000
Sweetener	Sodium saccharin	0.300

	Active	Sodium fluoride	0.306
	Flavour	Flavour	1.000
	Abrasive (hard)	Zeodent 124	1.330
	Abrasive (soft)	Zeodent 623	3.670
	Thickener	Zeodent 163	3.000
	pH adjuster	35% NaOH solution	0.250
	Dye	Dye	0.003
	Water	to	100.000

Example 3

Function	Component	wt%
Humectant	Sorbitol 70% non-crystallizing	28.000
Humectant	Glycerin	22.00
Suspending agent	PEG 6	2.500
Foaming agent	Empicol 0303 solid	1.500
Sweetener	Sodium saccharin	0.300
Active	Sodium fluoride	0.306
Flavour	Flavour	1.000
Abrasive (hard)	Zeodent 124	1.330
Abrasive (soft)	Zeodent 623	3.670
Thickener	Zeodent 163	3.000
Thickener	Xanthan (Keltrol F)	0.250
Dye	Dye	0.003
Water	to	100.000

This fluid formulation was made by a process as described above, involving

1. Adding a suitable quantity of water to a mixing vessel.
2. Adding sweetener and active to the water, mixing until dissolved using a circular Heidolph paddle stirrer.

3. Adding the glycerol and sorbitol to the batch, mixing until dissolved using a circular paddle stirrer on the Heidolph.

4. Sieving the abrasive to break up any lumps. A 500 micron sieve is generally suitable.

5. Slowly adding the abrasive to the mixture, mixing using a circular paddle stirrer on the Heidolph..

6. Slurrying the thickening agent and slurrying agent and add to the mixture, agitate until homogeneous.

7. Transferring to an Ultra Turrux mixer and mixing for 5 minutes.

8. Slurrying the flavour and foaming agent and adding to the mixture, mixing until homogeneous with a circular paddle stirrer on the Heidolph.

9. Adjusting the pH to pH 8 (+/- 0.5) using the NaOH.

10. Mixing until homogeneous using circular paddle stirrer on the Heidolph.

This fluid mixture was charged into valved containers together with the propellant mixture in a 95:5 w/w ratio.